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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/465,338	12/17/1999	Kenneth S. Albert	PT-1817	8786

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EXAMINER	
PULLIAM, AMY E	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/465,338	ALBERT ET AL.	
	Examiner	Art Unit	
	Amy E Pulliam	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-110* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *48,49 and 60* is/are allowed.

6)☒ Claim(s) *1-47,50-59 and 61-110* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt of Papers

Receipt is acknowledged of the Extension of Time, the Amendment E, and the Letter regarding the Priority Document, received by the Office August 19, 2002, August 19, 2002, and September 25, 2002, respectively.

Allowable Subject Matter

Claims 48, 49, and 60 are allowable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-15, 17, 19-37, 39, 43, and 63-78 are rejected under 35 U.S.C. 102(b) as being anticipated by EPA 856 313 to Geoghegan *et al.* ('313).

EPA '313 discloses a controlled absorption diltiazem pellet formulation for oral administration to control hypertension and angina comprising a core of diltiazem or a pharmaceutically acceptable salt thereof, and a multilayer membrane surrounding the core and containing both a water insoluble and a water soluble polymer (abstract). EPA '313 further discloses that the formulation is preferred as a once-daily product to be administered before bedtime, and to be released at the following rates:

a. from 0 to 35% after 2 hours

b. from 4 to 45% after 4 hours

c. from 30 to 75% after 8 hours

d. from 60 to 95% after 13 hours

e. not less than 85% after 24 hours.

These release rates overlap those claimed by applicant in the instant application. Further, EPA '313 teaches that the water insoluble polymer can be replaced by a copolymer of acrylic and methacrylic acid esters (p 28, claim 10), and that the water soluble polymer can be HPMC (p 28, claim 7). EPA '313 also teaches that the core may comprise an organic acid, a lubricant (p 5, l 15-29), and other pharmaceutically acceptable components. In addition, throughout the examples, EPA '313 teaches varying amounts of active ingredient, including 120, 240, and 90 mg. Further, EPA '313 teaches tablet, pellet, and capsule formulations (exs. 8, 14, 21). Although EPA '313 does not disclose the exact release rates claimed by applicant, the ranges claimed fall within the range disclosed by EPA '313, and therefore are rendered obvious by the reference.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant argues that the reference failed to reach the higher bioavailability when given at night, compared to applicant's claimed invention. Additionally, applicant argues that the reference failed to show better clinical efficiency when given at night. These arguments are not persuasive for the following reasons. Applicant's instant claims are composition claims. It is general practice that future intent limitations are not given merit in a composition claim. Therefore, the

limitation "for evening dosing every 24 hours" is not a patentable limitation when found in a composition claim. In order for this limitation to have patentable weight it would need to be rewritten in a method of administration format. For a composition claim to be patentable over the prior art there must be components in the actual composition which make it different from the composition of the prior art.

Applicant also argues that the comparison of release profiles between the prior art and the instant claims is not valid because the releases are performed in two different mediums. The examiner acknowledges that the releases are performed in two different mediums, however, the rejection is maintained. Applicant has provided no limitations into the claim which makes the actual composition and its components differ from the cited art. Therefore, the burden is shifted to applicant to show that the release profile of the prior art, in water, is different than applicant's claimed release profile. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. *See Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Lastly, applicant argues that the lower limits of the release rates are not the same. However, in order to anticipate the invention, the ranges need only overlap, so this argument is not persuasive.

If applicant's composition differs from the composition of the prior art, it is recommended that applicant insert into the claim language that additional components which make the compositions different. Future intended use limitations are not persuasive for the reasons state above. Additionally, release profile limitations are not persuasive, unless it can be shown, by applicant, that the cited art composition does not possess these same release characteristics. For the above reasons, this rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-47, 50-59, and 61-110 are rejected under 35 U.S.C. 103(a) as being unpatentable over EPA 856 313 to Geoghegan *et al.* ('313).

EPA '313 does not teach all of the specific amounts of Diltiazem present in the formulation, nor do they teach the specific wetting agent claimed by applicant. However, the formulation disclosed in EPA '313 does teach a varied range of the amount of active ingredient, as well as the presence of additional additives, such as lubricants. Further, the formulation also releases the drug at the same rate as that claimed by applicant, therefore, it appears that these limitations do not render any unexpected results. It is the position of the examiner that these are limitations which would be routinely determined by one of ordinary skill through minimal

experimentation, as being suitable, absent the presentation of some unusual and/ or unexpected results. The results must be based on the specific limitations.

Furthermore, it is the position of the examiner that EP '313 teaches the generic concept of the invention, as well as the suggestion to manipulate the formulation to result in varying dissolution rates and Cmax values. One of ordinary skill in the art would have been motivated to manipulate the formulation based on the specifics of the desired formulation. The expected result would be a successful pharmaceutical formulation. Therefore, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments have been fully considered but are not found persuasive. Applicant argues that attached references show that the prior art is not suitable for evening dosing. This argument has been discussed above. However, if there is something different in applicant's formulation which makes is suitable for evening dosing, while the cited art is not, it is recommended that these different components or ingredients be inserted into the claim language.

Additionally, applicant argues that the references Tmax is arrived at on the basis of the mean curve which accounts for two peaks, so Tmax actually isn't 14 hours. The examiner does not fully understand this argument. After again examining the cited reference, it teaches that the Tmax does fall within applicant's claimed range. Applicant further asserts that page 111 of an article shows Tmax to be 6.8+/- 1.1. The examiner can not locate the reference to which applicant is referring. However, this is unimportant, because the teachings of the cited reference

show that the Tmax falls within the claimed range. For these reasons, this rejection is maintained.

Claims 1-47, 50-59, 61, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/00093 to Deboeck *et al.* ('093). WO '093 discloses an extended release galenical form of Diltiazem or a pharmaceutically acceptable salt, with a wetting agent, coated with a microporous membrane comprising at least a water soluble polymer and a pharmaceutically acceptable adjuvant. WO '093 further teaches that the composition comprises beads containing between 120 and 480 mg of the active ingredient, with the wetting agent, and the beads are coated with the microporous membrane (p 19, claim 1). WO '093 further teaches that the water soluble polymer or copolymer can include HPMC and Eudragit (p 8, l 21-28). Further, WO '093 teaches that the following ingredients are included in the formulation: wetting agents such as fatty acid esters of saccharose (2-20%), microcrystalline cellulose (5-25%), polyvinylpyrrolidone (1-15%), titanium oxide, surfactants such as tween, antifoaming agents, magnesium stearate, and talc (see pages 8-10). These are the ingredients disclosed by applicant as being present in the formulation. WO '093 also teaches that the formulation is for once daily administration.

WO '093 does not teach the exact rates of release as claimed by applicant, nor do they discuss the rates of release after 8 hours, nor do they disclose all of the specific amounts of the above mentioned ingredients. However, WO '093 does teach overlapping rates of release to those claimed by applicant, and they do teach the same ingredients as claimed by applicant. It is the position of the examiner that the present application is not patentably distinct from WO '093,

as they contain the same ingredients, in the same formulation, with overlapping rates of release, even though WO '093 does not disclose the specific amounts of all the ingredients. It is the position of the examiner that the specific amounts of those ingredients which are not disclosed in WO '093 are limitations which would be routinely determined by one of ordinary skill in the art through minimal experimentation, absent the presentation of some unusual and/ or unexpected results. The results must be those that accrue from the specific limitations. Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to create a controlled release formulation of Diltiazem, based on the teachings of WO '093, and experiment with and vary the specific amounts of the ingredients, in order to achieve the desired rate of release.

Applicant argues that WO '093 does not teach the exact Cmax and Tmax as claimed by applicant. The examiner acknowledges this fact, and this is why the WO '093 reference is used as an obviousness reference, not an anticipation reference. It is the position of the examiner that because WO '093 contains the same ingredients in the same formulation, with overlapping release rates, applicant's invention is not patentably distinct from the prior art, therefore, this rejection is maintained.

Furthermore, applicant argues that the peak to trough variance for the WO '093 reference (which corresponds to Tiazac) is much larger than that of applicant's formulation. Applicant has provided evidence to reinforce this statement. However, the examiner respectfully disagrees as the data regarding Tiazac is concerning a 240 mg formulation, and the data regarding applicant's claimed formulation is based on a 300 mg capsule. Therefore, this comparison is not persuasive, and the rejection is maintained.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant argues that this reference does not teach the claimed Tmax values. The examiner does not find this argument persuasive because the reference teaches a sustained release composition, and the burden is hereby shifted to applicant to provide comparative data showing that the Tmax of the cited reference differs from applicant's claimed Tmax. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. *See Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). For these reasons, this rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E Pulliam whose telephone number is 703-308-4710. The examiner can normally be reached on Mon-Thurs 7:30-5:00, Alternate Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

A. Pulliam
Patent Examiner
Art Unit 1615
November 15, 2002

THURMAN K. PAGE
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